Relationship of hemodialysis access to finger gangrene in patients with end-stage renal disease

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Objective: **We report a comprehensive review of our patients on hemodialysis with end-stage renal disease (ESRD) with finger gangrene to determine etiology, natural history, and prognosis of this condition.**
Methods: **Patients with ESRD with finger gangrene were identified from our computerized vascular registry. Presence of an ipsilateral arteriovenous fistula was determined, and patients were compared with a group of patients with ESRD without finger gangrene. Management consisted of arteriography, selective arteriovenous fistula management, and finger amputation. A multivariate analysis to determine risk factors associated with finger gangrene was performed. Repeat finger amputation and survival rates were determined with life-table analysis.**
Results: **Twenty-three patients (mean age at start of dialysis, 53 years) with finger gangrene were identified, with 48% (n = 11) having a functional ipsilateral arteriovenous fistula. Arteriography was consistent with diffuse atherosclerosis involving the radial, ulnar, palmar, and digital arteries precluding attempts at distal arterial bypass. Repeat finger amputations were necessitated in 52% of patients (n = 12), and bilateral finger gangrene developed in 61% of patients (n = 14). Starting dialysis at age less than 55 years ($P = .0004$), diabetes ($P = .001$), coronary artery disease ($P = .0212$), and lower extremity arterial occlusive disease ($P < .0001$) were significantly associated with finger gangrene.**
Conclusion: **The young diabetic patient with diffuse vascular disease and ESRD is at high risk for the development of finger gangrene on chronic hemodialysis. Finger gangrene is the result of distal atherosclerosis and is not primarily related to dialysis access. (J Vasc Surg 2002;36:245-9.)**

Finger gangrene as the result of upper extremity arterial occlusive disease is a relatively infrequent clinical problem.[1] Only a minority of patients in our practice with finger gangrene have end-stage renal disease (ESRD). Questions frequently arise as to etiology of finger gangrene in these patients and relationship of the problem to an upper extremity hemodialysis access arteriovenous fistula or shunt. Objectively, little is known about the etiology, natural history, prognosis, and recommended management for these challenging cases.

Recent literature addressing the issue of hand ischemia in patients with ESRD on hemodialysis has been concerned with the treatment of hemodynamic steal syndrome induced by an arteriovenous shunt or fistula.[2,3] However, patients with ESRD with finger gangrene represent a more advanced and chronic form of upper extremity ischemia of which less is known concerning its relationship to a dialysis arteriovenous fistula or shunt. We are reporting herein a comprehensive review of our patients with ESRD on hemodialysis with finger gangrene to determine the etiology and natural history of this condition.

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PATIENTS AND METHODS

All patients with finger gangrene on chronic hemodialysis encountered (from January 1991 through December 2000) on our combined (Veterans Affairs Medical Center VAMC; University Hospital) vascular service were identified from a computerized patient registry. Patients with finger gangrene routinely were assessed for atherosclerotic risk factors and underwent bilateral upper extremity photoplethysmographic testing and angiography.[4] The gangrenous fingers could not be assessed with photoplethysmographic tracings; however, all other fingers were tested. Patients with ipsilateral functional upper extremity arteriovenous fistula underwent testing with and without compression of the fistula. Treatment consisted of digital amputation and selective arteriovenous fistula management. Patients were followed for the need for repeat finger amputation or hand amputation.

Patients on chronic hemodialysis at the Veterans Affairs Medical Center who were followed during the study period without finger gangrene served as a comparison group. Patients were identified from a database, and records were reviewed and assessed for the presence of atherosclerotic risk factors to include age, gender, diabetes, smoking history, hypertension, hyperlipidemia, lower extremity arterial occlusive disease (LED), and coronary artery disease (CAD). *LED* was defined as absent distal pulses to palpation or an ankle/brachial Doppler pressure index of less than 0.90. In addition, all study patients were assessed for age at initiation of dialysis and survival on dialysis.

Fig 1. Arteriogram shows diffuse atherosclerotic occlusive disease involving radial and ulnar arteries and incomplete diseased palmar arch and digital arterial occlusions.

Statistical analysis. Analysis of risk factors in patients with finger gangrene compared with other study patients was performed with χ^2 or Fisher exact tests for conditional variables and Student *t* test for continuous variables. A significant difference was assumed when *P* was less than .05. A multivariate analysis (one-way analysis of variance) to determine risk factors associated with finger gangrene also was performed. Patients also were assessed for survival, repeat finger amputation, and requirement for hand amputation. These results were calculated with the life-table method. In addition, survival rate from initiation of dialysis was calculated with the life-table method for patients with and without gangrene with differences determined with log-rank and χ^2 analysis.

RESULTS

During the 10-year study period, 23 patients with finger gangrene (mean age at initiation of dialysis, 53 years; range, 30 to 75 years; 20 male, three female) on chronic hemodialysis underwent management. In addition, 199 patients (mean age at initiation of dialysis, 63 years; range, 23 to 90 years; 195 male, four female) on chronic hemodialysis at the Veterans Affairs Medical Center without finger gangrene were followed. Patients with finger gangrene started dialysis at a significantly ($P = .001$) younger age (mean, 53 years) compared with patients without finger gangrene (mean, 63 years). Mean age at time of finger gangrene was 57 years. Mean time from the initiation of dialysis to finger gangrene was 36 months (range, 0 to 205 months).

Finger gangrene presented (14 patients right hand, six patients left hand, and three patients bilateral) initially ipsilateral to a dialysis fistula in 11 patients (48%), and in the other 12 patients (52%), initial finger gangrene presented in an extremity without a functional dialysis fistula. In five of these 12 patients, an occluded ipsilateral dialysis fistula had been nonfunctional for a mean of 21 months (range, 8 to 35 months) before the onset of finger gangrene. In patients with finger gangrene, the digital photoplethysmographic/brachial indexes were consistently abnormal with evidence for bilateral infrabrachial arterial occlusive disease (right hand: mean, 0.51; range, 0.23 to 0.88; left hand: mean, 0.49; range, 0.21 to 0.92).

Arteriography in all patients showed distal radial or ulnar disease and severe palmar and digital arterial disease (Fig 1). No patient had a distal target artery acceptable for bypass, although two patients underwent proximal brachial artery bypass and one patient underwent a distal revascularization interval ligation (DRIL) procedure. In six of 11 patients with finger gangrene ipsilateral to a dialysis fistula, the fistula was either ligated (n = 4) or spontaneously thrombosed (n = 2). The remaining five patients with functional ipsilateral fistula included one patient with a DRIL procedure, two patients with bilateral gangrene, and two patients who survived only a few months. In each case, no significant improvement was seen in measured digital photoplethysmographic/brachial indexes or angiographic hand circulation after fistula compression. Alternative methods for dialysis in the other 18 patients without functional ipsilateral fistula included central vein catheter in 11 patients, peritoneal dialysis in three patients, groin arteriovenous fistula in two patients, chest wall arteriovenous fistula in one patient, and contralateral upper extremity arteriovenous fistula in one patient.

All patients with finger gangrene underwent initial treatment with distal finger amputation of one or more digits. During follow-up (mean, 12 months), 14 patients (61%) had finger gangrene in their previously unaffected hand and 12 (52%) needed repeat finger amputation, ranging from two to five procedures per patient, totaling one to

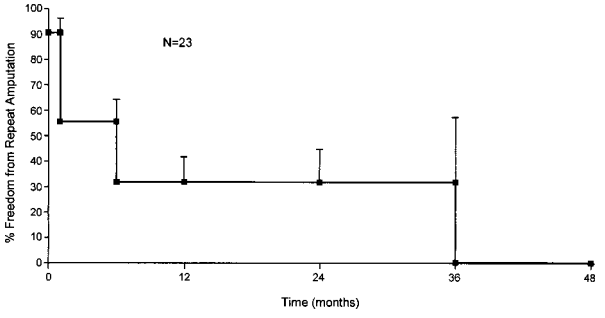

Fig 2. Life table shows rate of freedom from repeat finger amputation.

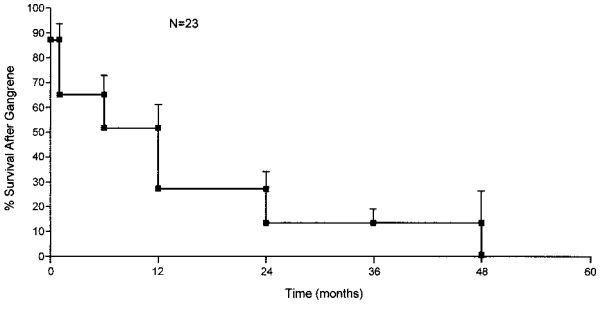

Fig 3. Life table shows patient survival rate after onset of finger gangrene.

six fingers amputated. No patients needed hand amputation. At 2 years, the rates of freedom from repeat finger amputation and hand amputation were 32% and 100%, respectively (Fig 2). Patient survival rate after the onset of finger gangrene was 27% at 2 years (Fig 3).

The incidence of atherosclerotic risk factors associated with finger gangrene in patients on hemodialysis is shown in the Table. The presence of diabetes, LED, and CAD and age less than 55 years at the start of dialysis were all significantly associated with the development of finger gangrene while on dialysis. Multivariate analysis was carried out after excluding LED because of overlap with CAD and diabetes. With multivariate analysis, CAD ($P = .0271$), diabetes ($P = .0030$), and age less than 55 years at the start of dialysis ($P < .0001$) were all significantly associated with finger gangrene. The 3-year survival rate on dialysis was 52% in the patients with finger gangrene compared with 49% in the patients without finger gangrene ($P > .05$; Fig 4).

LED was present in altogether 91 patients studied (41%), including all 23 patients with finger gangrene and 68 of 199 patients without finger gangrene (34%). LED was documented before the onset of dialysis in 21 of 23 patients with finger gangrene (91%) and in 57 of the 68 patients in the comparison group (84%). Sixteen of the 23 patients with finger gangrene (70%) needed lower extremity revascularization compared with 25 of 68 patients in the comparison group with LED (37%). Of the 41 patients with LED who underwent lower extremity revascularization, 24 patients (59%) needed arterial bypass while on chronic hemodialysis. Sixteen of the 23 patients with finger gangrene (70%) underwent at least one major lower extremity amputation compared with 22 of the 199 patients in the comparison group ((11%; $P < .05$).

DISCUSSION

The occurrence of hand ischemia in patients on chronic hemodialysis is well described. However, most attention by vascular surgeons has focused on the steal phenomenon caused by upper extremity arteriovenous fistulas resulting in the rather abrupt onset of global hand ischemia. The DRIL procedure has been recommended by several authors as a method to correct the steal phenomenon and preserve function of the arteriovenous fistula.[2,3] Finger gangrene is a more advanced form of hand ischemia encountered in the chronic hemodialysis population, which surprisingly in our experience was unrelated to a functional arteriovenous fistula in 52% of cases. However, ipsilateral arteriovenous fistula was clearly a contributing factor to the problem in at least five cases, with four shunts necessitating ligation and one DRIL procedure performed. It is noteworthy that, during follow-up and after selective fistula management, altogether 52% of patients returned with new digital gangrene necessitating repeat finger amputation procedures and 61% of patients had bilateral digital gangrene develop.

Uniformly, patients with finger gangrene were found to have distal atherosclerotic disease not amenable to revascularization.[5] Angiography consistently showed a diffuse occlusive process involving the distal radial or ulnar arteries and extending into the palmar and digital circulation. The process was bilateral and symmetrical and had an angiographic appearance consistent with atherosclerotic occlusive disease. Not surprisingly, our patients with finger gangrene had significantly more clinical evidence for total body atherosclerosis compared with those patients on chronic hemodialysis in whom finger gangrene did not develop. It is notable that 100% of our patients with finger gangrene had clinical evidence for LED, with 70% needing major lower extremity amputation compared with only 34% and 11%, respectively, in the comparison group ($P < .05$). In addition, the patients with finger gangrene had significantly higher prevalence rates of diabetes and CAD compared with the other patients on chronic hemodialysis.

Our data suggest that the relatively young (<55 years) diabetic patient with ESRD with diffuse vascular disease is at high risk for the eventual development of finger gangrene while on chronic hemodialysis. Although it was not objectively assessed in our study, a number of our patients with finger gangrene were known to have symptomatic atherosclerotic disease at an age younger than 45 years. Patients with premature atherosclerosis are reported to have high mortality and amputation rates and decreased vascular graft patency rates.[6] The mean time on dialysis before the development of finger gangrene was 36 months. Although rate of survival on dialysis was no different for

Table I. Simple associations of characteristics of patients for hemodialysis with development of finger gangrene

Variable (trait)	*No. of all patients (n = 222) with trait (%)*	*No. of patients with no finger gangrene (n = 199) with trait (%)*	*No. of patients with finger gangrene (n = 23) with trait (%)*	P *value*
Age < 55 years	63 (28)	50 (25)	13 (57)	.0004
Smoking history	205 (92)	185 (93)	20 (87)	NS
Male gender	215 (97)	195 (98)	20 (87)	NS
Diabetes	121 (55)	101 (51)	20 (87)	.001
HTN	205 (92)	185 (93)	20 (87)	NS
CAD	133 (60)	115 (58)	18 (78)	.0212
LED	91 (41)	68 (34)	23 (100)	<.0001
HL	60 (27)	53 (27)	7 (30)	NS

P value, from χ^2 analysis comparing patients with versus patients without trait in proportion of group having finger gangrene.
NS, Not significant; *HTN*, hypertension; *HL*, hyperlipidemia.

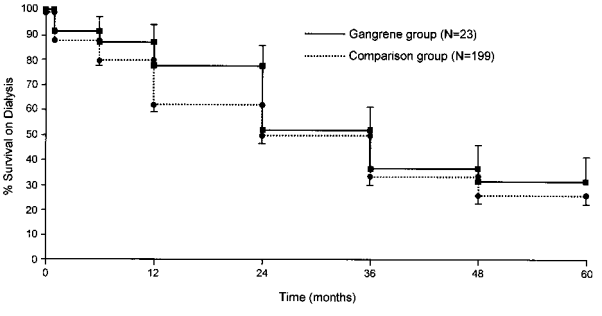

Fig 4. Life table shows patient survival rate after onset of dialysis for patients with finger gangrene compared with patients without gangrene.

patients in whom finger gangrene developed compared with other patients on chronic hemodialysis, the 2-year survival rate once finger gangrene developed was only 27%.

Chronic hemodialysis appears to accelerate the atherosclerotic process, although little is objectively known about the pathophysiology of this phenomenon. Patients on chronic hemodialysis are well documented to have high plasma homocysteine levels, and elevated plasma homocysteine levels have been associated with progression of vascular disease.[7-9] Also, lipoprotein (a), another well known atherosclerotic risk factor, is elevated in patients with ESRD.[6,10] In addition, an environment of increased oxidant stress has been postulated in patients on chronic hemodialysis, resulting in acceleration of the baseline atherosclerotic process.[11,12] Besides development of finger gangrene, it is notable that 59% of our patients with LED needed lower extremity revascularization while on chronic hemodialysis. These data document progression of both upper and lower extremity vascular disease in our hemodialysis patient population.

Our series lacks data on hand blood supply in patients at the onset of hemodialysis. In addition, our series is somewhat atypical because it reflects the male-predominant dialysis population that we serve. It appears, however, that the young diabetic patient with ESRD and clinical evidence for diffuse vascular disease is at significant risk for progressive atherosclerosis and the development of finger gangrene. These patients should be counseled regarding their risk and should undergo predialysis noninvasive testing to include bilateral upper extremity pulse examination and finger photoplethysmographic pressures. Upper extremity fistulas or shunts, if used, should be thoughtfully planned, and patients should have careful long-term longitudinal follow-up and monitoring for the development of digital ischemia, including finger photoplethysmographic pressures with and without fistula compression.

Patients with ESRD with finger gangrene should undergo angiography even though distal revascularization is rarely possible. Angiography may identify significant proximal arterial disease and document the extent of the distal occlusive process. Also, patients with ipsilateral fistula can undergo angiography with and without fistula compression to assess for improvements in hand blood flow, which helps select those patients who will benefit from fistula ligation or, rarely, a DRIL procedure. Nonetheless, in most cases, our clinical experience and angiographic findings indicate that finger gangrene in patients with ESRD is primarily related to severe distal atherosclerosis and not ischemic steal syndrome.

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DISCUSSION

Dr Spencer Galt (Salt Lake City, Utah). Dr Yeager and his colleagues from Portland have brought to our attention an uncommon but vexing clinical problem. In this paper, they have reviewed their local experience in the evaluation and management of patients with end-stage renal disease presenting with finger gangrene. They accurately point out that relatively little is known about the etiology, natural history, prognosis, and management of this challenging group of patients.

This study identified 23 patients over a 10-year period with finger gangrene on the combined vascular surgery services at the Portland VA and University Hospital. Each of these patients was undergoing chronic hemodialysis. Although we are not told the denominator, this presumably represents a small minority of all patients undergoing dialysis at the two hospitals.

I suspect that most of us would anticipate that the finger gangrene was related, at least in part, to steal from an upper-extremity fistula. However, we are told that fewer then half of these patients initially presented with gangrene ipsilateral to the dialysis fistula. Nevertheless, among the 10 patients in whom the gangrene was ipsilateral to the fistula, one underwent a DRIL procedure, and in three the fistula was ligated. In two additional patients, the fistulae thrombosed, although presumably not as part of a management plan. Therefore, in some of these patients, the managing surgeon felt that steal was likely playing a role in the gangrene. This brings me to my first question. While you mentioned that patients underwent noninvasive testing, did that always include with and without compression of the fistula? If so, was there any evidence of increased hand perfusion with the fistula compressed? Further, do you have any noninvasive data on hand perfusion in these patients prior to the institution of dialysis?

Univariate analysis revealed that age of onset of dialysis <55 years, diabetes, the presence of CAD, and LEOD were significantly associated with the development of finger gangrene. As you point out in the discussion in the manuscript, chronic hemodialysis appears to accelerate the atherosclerotic process. Nevertheless, most patients on hemodialysis do not develop finger gangrene. Would you please speculate for us what makes these patients more susceptible to such severe and diffuse atherosclerosis?

The group from Portland has once again shed light on a difficult clinical situation that most of us will encounter from time to time. While the data suggest that there is little we can offer to preserve fingers and prevent the progression of gangrene, these patients fortunately remain free of major upper-extremity amputation during their short remaining life. I thank the Society for inviting me to discuss this paper.

Dr James M. Edwards. Dr Galt, thank you for your comments. In response to your questions I have the following comments.

First, most of the upper-extremity vascular tests were done with and without fistula compression, and there often was little increase in finger pressure with the graft occluded. It is our impression that this phenomenon is due to the severe and widespread palmar and digital artery occlusive disease seen in these patients. This finding reinforced our impression that the finger gangrene seen in these patients was not due to a hemodynamic steal from an arteriovenous fistula. We do not have data on what the hand circulation in these patients was like prior to the institution of dialysis.

Your second question is more difficult to answer. I do not know why some patients on dialysis develop finger gangrene. In my experience there is a bimodal distribution with a few patients developing finger ischemia early secondary to a hemodynamic steal from an arteriovenous fistula, and then another group developing finger ischemia late due to severe distal atherosclerosis, which is the group we are describing. Our data demonstrate that this group is younger, so perhaps they have an increased number of or more severe comorbidities that lead to the early institution of dialysis and that also lead to rapid and severe atherosclerosis.